Ron S. Israeli et al.

Serial No.: Filed :

08/403,803

Page 2

March 17, 1995

- b) contacting the mRNA sample under hybridizing conditions with a labeled nucleic acid probe which:

  (1) is at least 15 nucleotides in length and (2) hybridizes specifically to a nucleic acid having a sequence which is complementary to a sequence present in the sequence set forth in SEQ ID NO. 1.-
- c) removing any unbound labeled nucleic acid probe; and
- d) detecting the presence of labeled nucleic acid probe hybridized to the mRNA so as to thereby detect micrometastic prostate tumor cells in the subject.--

--98.

--99.

(New) A method of detecting micrometastic prostate tumor cells in a subject which comprises:

- a) obtaining a suitable sample of mRNA from the subject;
- b) reverse transcribing the mRNA to generate a single -stranded cDNA;
- c) contacting the single-stranded cDNA under hybridizing conditions with a labeled nucleic acid probe which: 1) is at least 15 nucleotides in length; and 2) hybridizes specifically to a nucleic acid having a sequence set forth in SEQ ID NO:1;--
- d) removing any unbound labeled nucleic acid probe; and
- e) detecting the presence of labeled nucleic acid probe hybridized to the cDNA so as to thereby detect detect m crometastic prostate tumor cells in the subject.--

(New) A method of detecting micrometastic prostate tumor

Lant Cont

Ron S. Israeli et al.

Serial No.:

08/403,803

Filed Page 3

March 17, 1995

cells in a subject which comprises:

a) obtaining a suitable sample of mRNA from the subject;

- b) generating a double-stranded mRNA-cDNA duplex from the mRNA;
- c) contacting the duplex from (b) with one primer having a sequence which is complementary to a portion of the sequence set forth in SEQ ID NO:1 and a second primer having a sequence which comprises a different portion of the sequence set forth in SEQ ID NO:1;
- d) amplifying the nucleic acid from (c) using a polymerase chain reaction to obtain an amplification product;
- e) contacting the amplification product of (d) under hybridizing conditions with a labeled nucleic acid probe which: 1) is at least 15 nucleotides in length; 2) hybridizes specifically to a nucleic acid having a sequence set forth in SEQ ID NO. 1.;
- f) removing any unbound labeled nucleic acid probe; and
- g) detecting the presence of labeled nucleic acid probe hybridized to the amplification product so as to thereby detect micrometastic prostate tumor cells in the subject.--

--100. (New) A method of detecting micrometastic prostate tumor cells in a subject which comprises:

- a) obtaining a suitable sample of mRNA from the subject;
- b) generating a double-stranded mRNA-cDNA duplex from the mRNA;
- c) contacting the duplex from (b) with one primer

Subcent Applicants: Serial No.: Filed : Page 4 Ron S. Israeli et al.

08/403,803 March 17, 1995

having a sequence which is complementary to a portion of the sequence set forth in SEQ ID NO:1 and a second primer having a sequence which comprises a different portion of the sequence set forth in SEQ ID NO:1;

- d) amplifying the nucleic acid from (c) using a polymerase chain reaction to obtain an amplification product;
- e) contacting the amplification product of (d) under hybridizing conditions with a labeled nucleic acid probe which: 1) is at least 15 nucleotides in length; and 2 hybridizes specifically to a nucleic acid having a sequence complementary to the DNA sequence set Forth in SEQ ID NO:1.;
- f) removing any unbound labeled nucleic acid probe; and
- g) detecting the presence of labeled nucleic acid probe hybridized to the amplification product so as to thereby detect micrometastic prostate tumor cells in the subject.--

(New) A method of detecting the presence of a nucleic acid encoding a prostate specific membrane antigen in a subject which comprises:

- a) obtaining a suitable sample of mRNA from the subject;
- b) generating a double-stranded cDNA from the mRNA;
- c) contacting the double-stranded cDNA from (b) with one primer having a sequence which is complementary to a portion of the sequence set forth in SEQ ID NO:1 and a second primer having a sequence which comprises a different portion of the sequence set forth in SEQ ID NO:1;

Sult Juni

E --101.

Ron S. Israeli et al.

Serial No.: Filed :

08/403,803 March 17, 1995

Page 5

d) amplifying the double stranded cDNA using a polymerase chain reaction to obtain an amplification product;

- e) contacting the amplification product of (d) under hybridizing conditions with a labeled nucleic acid probe which 1) is at least 15 nucleotides in length; 2) hybridizes specifically to a nucleic acid having a sequence complementary to the DNA sequence set forth in SEQ ID NO:1.;
- f) removing any unbound labeled nucleic acid probe; and
- g) detecting the presence of labeled nucleic acid probe hybridized to the amplification product so as to thereby detect the presence of a nucleic acid encoding a prostate specific membrane antigen in a subject.--
- --102. (New) A method of detecting the presence of a nucleic acid encoding a prostate specific membrane antigen in a subject which comprises:
  - a) obtaining a suitable sample of mRNA from the subject;
  - b) generating a double-stranded cDNA from the mRNA;
  - c) contacting the double-stranded cDNA from (b) with one primer having a sequence which is complementary to a portion of the sequence set forth in SEQ ID NO:1 and a second primer having a sequence which comprises a different portion of the sequence set forth in SEQ ID NO:1;
  - d) amplifying the double stranded cDNA using a polymerase chain reaction to obtain an amplification product;

Ent

Ron S. Israeli et al.

Serial No.:

08/403,803

Filed

March 17, 1995

Page 6

e) contacting the amplification product of (d) under hybridizing conditions with a labeled nucleic acid probe which 1) is at least 15 nucleotides in length; 2) hybridizes specifically to a nucleic acid having a sequence set forth in SEQ ID NO:1.;

- f) removing any unbound labeled nucleic acid probe; and
- g) detecting the presence of labeled nucleic acid probe hybridized to the amplification product so as to thereby detect the presence of a nucleic acid encoding a prostate specific membrane antigen in a subject.--

--103.

(New) The method of any one of claims 97-102, wherein the sample is blood, lymph nodes, or bone marrow. --

## Remarks

Claims 90-96 were pending in the subject application. Applicants have hereinabove canceled claims 90-96 without prejudice to applicants right to pursue the subject matter of these claims in a later-filed application and add new claims 97-103. Support for claims 97-103 may be found inter alia in the specification as follows: claims 97-102: page 23, lines 9-13; page 23, lines 21-30; page 24, line 22; page 25, lines 28-29; page 39, lines 25-35; page 45, lines 28-29; page 47, line 20; page 87, line 33; page 90, line 5 to page 92, line 20; page 91, lines 5-15; claim 103: page 136, lines 25-35. Claims 97-103 do not involve any issue of new matter such that entry of this amendment is respectfully requested.

## Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 90-93 under 35 U.S.C. §112, first